510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
DEVICE AND INSTRUMENT TEMPLATE

A. 510(k) Number:
k040332

B. Purpose for Submission:
To obtain 510(k) clearance in a Physician's Office Laboratory (POL) setting.

C. Analyte:
Alanine amino transferase (ALT/SGPT) test system.

D. Type of Test:
Quantitative

E. Applicant:
POLYMEDCO, INC.

F. Proprietary and Established Names:
POLYMEDCO SPOTCHEM EZ CHEMISTRY ANALYZER

G. Regulatory Information:

1. Regulation section:
   21CFR §862.1030 -Alanine amino transferase (ALT/SGPT) test system.
   21CFR §862.2170 -Micro chemistry analyzer for clinical use.
2. Classification:
   Class 1 meets the limitations of exemptions 862.9 (c) (9)
3. Product Code:
   CKA, JJF
4. Panel:
   Chemistry (75)

H. Intended Use:
1. Indication(s) for use:
   The Polymedco SpotChem EX and ALT test system is an in vitro diagnostic instrument and procedure intended to measure the enzyme alanine amino transferase or ALT (also known as a serum glutamic pyruvic transaminase of SGPT) in serum plasma and whole blood. ALT measurements are used in the diagnosis and treatment of certain liver diseases (e.g., viral hepatitis and cirrhosis) and heart diseases.
2. Special condition for use statement(s):
   Prescription Use
3. Special instrument Requirements:
   Polymedco SpotChem EX

I. Device Description:
The Polymedco SPOTCHEM EZ ALT test system is an in vitro diagnostic procedure intended to measure alanine amino transferase (ALT) quantitatively in human serum, plasma, and whole blood on the SPOTCHEM EZ (SP-4430) analyzer.

The SPOTCHEM EZ ALT Reagent Strip is composed of a plastic strip to which a multi-layered test field is affixed. The layers consist of a sample-retention layer, a layer containing the reagents and a support layer.
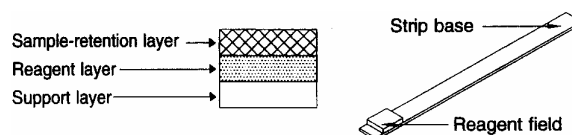
The patient sample (serum, plasma, or whole blood) is placed in a disposable sample cup and installed in the centrifuge of the SPOTCHEM EZ analyzer. When the analyzer is activated the sample is automatically centrifuged to remove the solid fraction. After centrifugation the analyzer removes a portion of the cell-free supernatant and automatically delivers it to the reagent test strip. A fixed amount of supernatant is placed on the test field of the reagent strip. The supernatant spreads in a uniform fashion across the entire surface of the sample retention layer. The supernatant then permeates into the reagent layer where the reaction is initiated.

J. Substantial Equivalence Information:
1. <u>Predicate device name(s):</u>
   Polymedco Poly-Chem System, Alanine Aminotransferase (ALT)
2. <u>Predicate K number(s):</u>
   k020852/A010
3. <u>Comparison with predicate:</u>

   Similar colorimetric enzyme-based methods for determining ALT levels are well established. The modified NADH oxidation/NAD reduction method for ALT detection used in the SPOTCHEM EZ analyzer is based on several predicate devices. Examples are, but are not limited to: Trace Reagent Line for the COBAS Mira (k973869); HiChem ALT Reagent Kit (k 951818); **Polymedco's Poly-Chem ALT Kit (k020852/A010)**; Roche Reagent for ALT (k 924245); and COBAS Ready Stat Profile Reagent Strip (k 896234).

   The similarities of these in vitro diagnostic test methods are summarized as follows:
   a) All tests are based on a modified NADH oxidation/NAD reduction method for colorimetric detection of the ALT present.
   b) All of these tests may use serum and/or plasma patient sample; the SPOTCHEM EZ ALT Test may also use whole blood specimens (as well as serum or plasma), but the SPOTCHEM EZ instrument automatically centrifuges the sample prior to addition onto the reagent test strip; only the cell-free supernatant is added to the reagent test strip.
   c) All tests make use of a calibrator to verify the stability of the reagents.
   d) All products recommend the use of controls.
   e) In a correlation utilizing 40 samples with the **Polymedco Poly-Chem System, Alanine Aminotransferase (ALT) kit** the regression equation was $y = 0.991x - 7.602$ and the $r = 0.999$
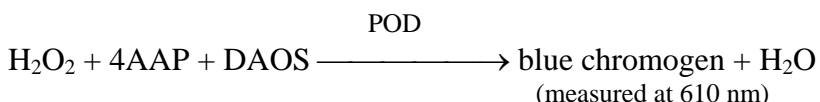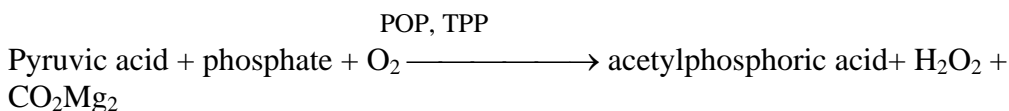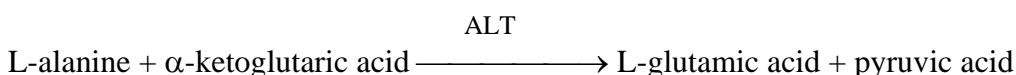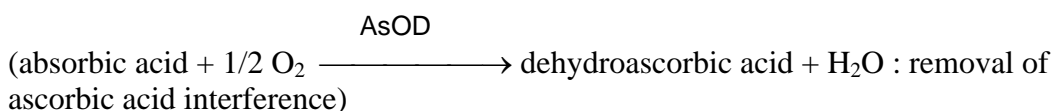
K. Standard/Guidance Document Referenced (if applicable):

None referenced

L. Test Principle:

ALT in the sample transfers amino group of L-alanine to a-ketoglutaric acid and produces L-glutamic acid and pyruvic acid. The pyruvic acid, in the presence of magnesium ion and thiamine pyrroline, is oxidized by the catalytic action of pyruvic acid oxidase, to produce hydrogen peroxide.) The hydrogen peroxide oxidizes and condenses 4-aminoantipyrine (4AAP) and DAOS by the catalytic action of peroxidase to form a blue color.

During the reaction, the reagent layer is completely dissolved and is absorbed by the sample-retention layer. These two layers thus form a single detection layer. The rate at which the blue color is generated in this detection layer is proportional to the ALT activity in the patient sample.

$$(\text{absorbic acid} + 1/2\ O_2 \xrightarrow{\text{AsOD}} \text{dehydroascorbic acid} + H_2O : \text{removal of ascorbic acid interference})$$

$$\text{L-alanine} + \alpha\text{-ketoglutaric acid} \xrightarrow{\text{ALT}} \text{L-glutamic acid} + \text{pyruvic acid}$$

$$\text{Pyruvic acid} + \text{phosphate} + O_2 \xrightarrow{\text{POP, TPP}} \text{acetylphosphoric acid} + H_2O_2 + CO_2Mg_2$$

$$H_2O_2 + 4AAP + DAOS \xrightarrow{\text{POD}} \text{blue chromogen} + H_2O$$
$$(\text{measured at 610 nm})$$

The intensity of the blue chromogen as measured at 610 nm by reflectance spectro-photometry is directly proportional to the ALT concentration in the patient sample. After the completion of the measurement, the SPOTCHEM EZ analyzer calculates the concentration of ALT [D] as follows:

$$D = a \cdot (K/S)^3 + b \cdot (K/S)^2 + c \cdot (K/S) + d$$

Where (K/S) is the Kubelka-Munk value for reflectance and a, b, c and d are coefficients derived from the calibration curve.

M. Performance Characteristics (if/when applicable):

1. <u>Analytical performance:</u>
    a. *Precision/Reproducibility:*
       Intra assay Precision
       Intra assay precision (within run) was assessed at three levels: below the normal range, within the normal range and above the normal range on the SPOTCHEM EZ analyzer. Twenty replicates of the same sample within one analytical run were evaluated at three levels. The mean, standard deviation (SD) and coefficient of variation (CV) in percent were calculated. An intra assay CV of < 5% was determined to be acceptable.

Intra Assay Precision ALT on SPOTCHEM EZ Analyzer. Results reported in IU/L.

| ANALYZER SPOTCHEM EZ	LEVEL 1	LEVEL 2	LEVEL 3
N=	20	20	20
Mean=	19.85	99.6	180
SD=	0.988	2.722	3.464
%CV=	4.98	2.73	1.92

Inter Assay Precision
Inter assay (between run) precision was determined by analyzing three different samples in each of four different runs repeated over five different occasions. An inter assay CV of <10% was determined to be acceptable.

Inter Assay Precision ALT on SPOTCHEM EZ Analyzer. Results reported in IU/L.

ANALYZER SPOTCHEM EZ	LEVEL 1	LEVEL 2	LEVEL 3
Days	5	5	5
n=	20	20	20
Mean=	20.6	103.2	173.15
SD=	0.883	6.221	3.897
%CV=	4.28	6.03	2.25

   b. *Linearity/assay reportable range:*
      Linearity/calibration curve fit data was generated for a pool that spanned the linear range of the test. Serial dilution sets were prepared using 0.9% saline solution and made up fresh and assayed with each of three calibrated runs. The results at each level of analyte were averaged and the linear fit was assessed. The linearity claim is based on a percent deviation of not more than 10% at the two highest analyte concentrations. The measured ALT was found to be linear up to 1200 IU/L.

$y = 0.991x + 7.602 \qquad r^2 = 0.998$
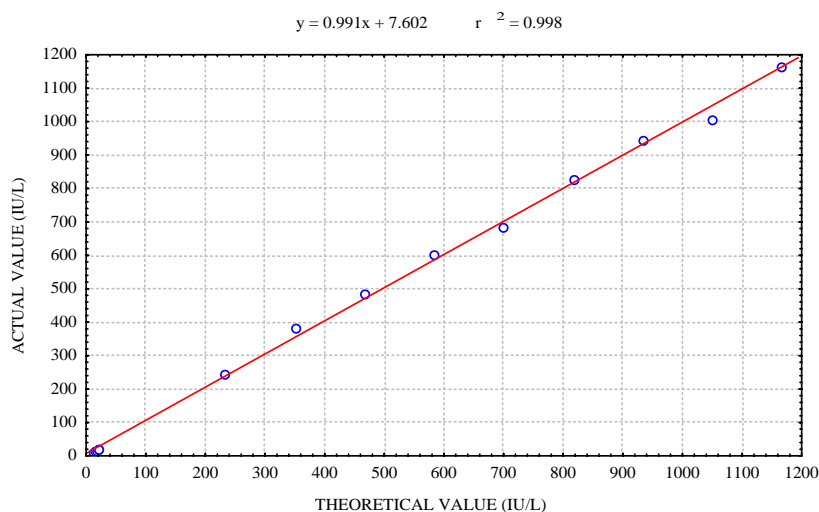
c. Traceability (controls, calibrators, or method):
The calibration set points are fixed by the manufacturer and are unique with each reagent lot and stored on the magnetic card provided with each kit lot. The calibration of the ALT assay is traceable to European Reference Materials.

Calibration is recommended with a change of reagent test strip lot or as indicated by internal procedures. A lot-specific calibration Reagent Card is supplied with each kit.

The principle of the calibration is to fix a two-point calibration curve for a given lot into the memory of the instrument. The sample absorbances are then read off this fixed curve by the instrument and the concentration is calculated and the results are provided by the software.

The magnetic card has values of the basic calibration curve (Cal-Low (a), and Cal-High (b)) and its own measured value (Cal-Low (A), and Cal-High (B)).

During calibration, the SpotChem EZ reads these 4 values from each magnetic card and calculates the calibration to be A->a, B->b. To assign A and B: average on n=18 tests x High (for B) and Low (for A) in each loth with Calibrator. a and b: Indicated value of calibrator.

The value of calibrator is assigned by the manufacturer by assessing the mean value of 3 lots x n=6 x 5 days x 2 instruments x High (for b) and Low (for a).

Control values are determined using previously cleared control material (K942458). The value assignment protocol is as follows: a minium of five vials of each control level is required for value assignment. One vial is required for each day, and will be tested on three different instruments to produce a minimum of 10 replicates on each instrument. Each instrument will be calibrated each testing day for five testing days.

d. *Detection limit:*
Functional sensitivity was assessed by diluting a pool to 6 different concentrations below the lower limit of the normal ALT range. Three runs were performed over three different days on the SPOTCHEM EZ. The mean, standard deviation and percent coefficient of variation was calculated for the ten replicates of each dilution. The functional sensitivity of the triglyceride test was defined at the value of the dilution where the CV is approximately 20% (taking into consideration that the actual mean was within + 10% of the expected target). It was determined that the functional sensitivity was 12.30 IU/L with a CV reported at 6.7%.

e. *Analytical specificity:*
The principle of the interference studies is to establish the level at which the interfering substance will cause a significant increase or decrease in the reagent's performance. The acceptable criteria established are that the analyte recovery should not vary from the base recovery by less or more than 10%. The interference studies were performed on samples with ALT concentrations of approximately 20, 50, 120 mg/dl..
• Interference was shown at or above 300 mg/dL of Hemoglobin.
• Interference was shown at or above 3.0 mg/dL of Bilirubin.
• Interference was shown at or above 200 mg/dL of Triglyceride.

f. *Assay cut-off:*
Not Applicable

2. <u>Comparison studies:</u>
a. *Method comparison with predicate device:*
A clinical correlation study was performed comparing the ALT test results generated on the SPOTCHEM EZ analyzer against the results generated from the Polymedco Poly-Chem System, Alanine Aminotransferase (ALT) Test performed on the Poly-Chem Chemistry Analyzer. The 40 samples spanned from 3 IU/L to 103 IU/L. The regression equation was y = 1.080x - 1.768 and the r = 0.986.

$y = 1.080x - 1.768$ $r^2 = 0.971$
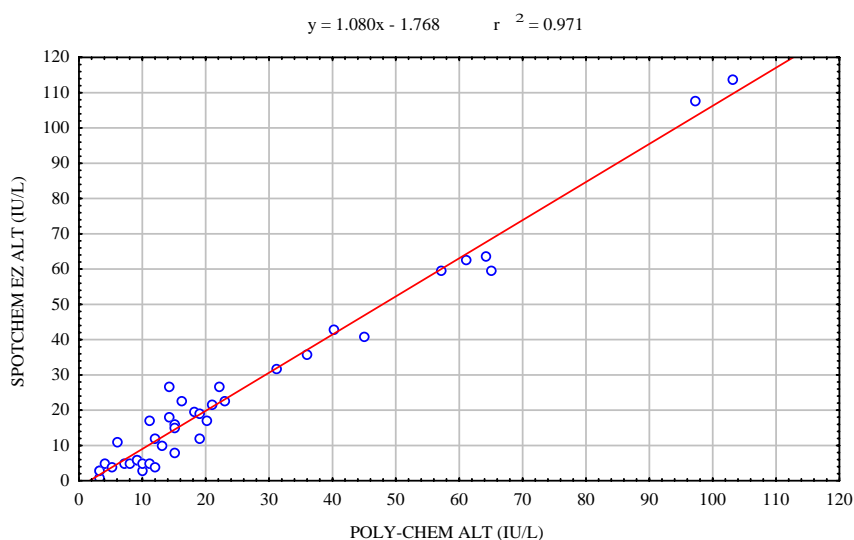
b. *Matrix comparison:*
    A clinical correlation study was performed comparing the ALT test
    results generated from plasma specimens against the results
    generated from whole blood specimens when performed on the
    SPOTCHEM EZ Analyzer. The 33 samples spanned from 1 IU/L to
    498 IU/L. The regression equation was y = 1.004x + 1.438 and r =
    0.9998.

$y = 1.004x + 1.438$ $r^2 =$
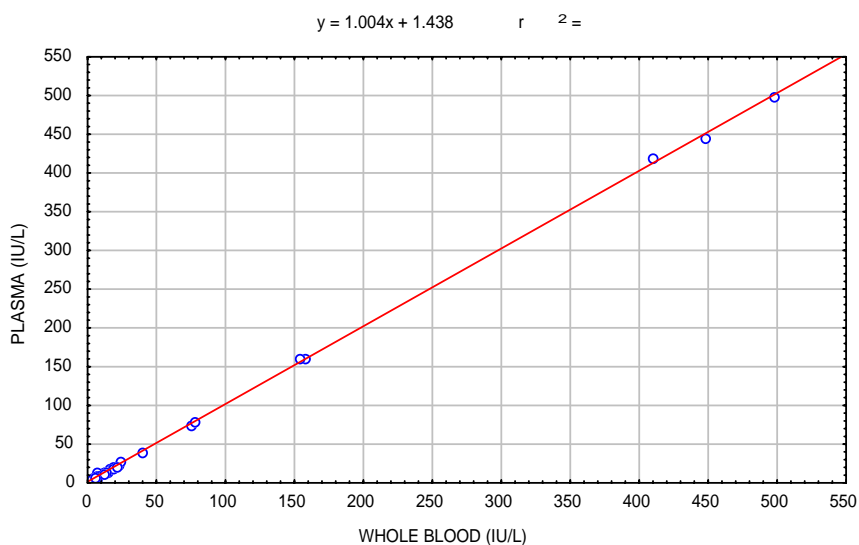
3. <u>Clinical studies:</u>
    a. *Clinical sensitivity:*
        Not Applicable
    b. *Clinical specificity:*
        Not Applicable

      c. Other clinical supportive data (when a and b are not applicable):
POC study – designed to assess the ability of the intended population of users (subject with no laboratory experience) to effectively use the SpotChem EZ instrument by following the package insert instructions and assaying three samples. Sixty subjects were recruited and the study was conducted at three sites. Precision in the hands of lay users for two samples was shown to be equivalent the predicate device. One sample could not be evaluated for precision because the level was below the assay reportable range, however this demonstrates expected results.

4. Clinical cut-off:
    Not Applicable
5. Expected values/Reference range:
    REFERENCE VALUES[1,2]

Specimen Type	IU/L	μkat/L
Blood, Serum, plasma[3,4]	< 33	< 0.55

	25°C	30°C	37°C
Men	up to 22 IU/L	up to 29 IU/L	up to 40 IU/L
Women	up to 17 IU/L	up to 22 IU/L	up to 31 IU/L

1. Wallnofer H, Schmidt.E, Schmidt FW, eds: Synopsis der Leberkrankheiten Stuttgart, Georg Thieme Verlag, 1974.
2. Thefeld W, et al: Dtsch Med Wschr 1974; 99: 343.
3. Bach N, Koff RS, Maddrey W: MLO. 2000 Jun;32(6):58-64
4. Kaplan MM: Ann Intern Med (US), 2002 Jul 2;137(1):49-51

N. Instrument Name:
Polymedco SpotChem EX

O. System Descriptions:

1. Modes of Operation:
    Single sample – single strip reagent and multistrip (6) reagent capabilities
2. Software:
    FDA has reviewed applicant's Hazard Analysis and software development processes for this line of product types:
    Yes ___X___ or No _____
3. Sample Identification:
    Manual or barcode entry no direct sample ID
4. Specimen Sampling and Handling:
    Single manual loading serum/plasma/whole blood capability to a centrifuge cup for auto-centrifugation
5. Assay Types:
    Reflectance spectro-photometry

6. <u>Reaction Types</u>:
   NADH oxidation/NAD reduction method
7. <u>Calibration</u>:
   Magnetic strip reagent lot specific 2 point adjustment
8. <u>Quality Control</u>:
   Recommend daily quality control no quality control data processing capabilities

P. Other Supportive Instrument Performance Characteristics Data Not Covered In The "L. Performance Characteristics" Section Of The SE Determination Decision Summary:

The instrument is UL approved as a Laboratory Use Electrical Equipment

Q. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.